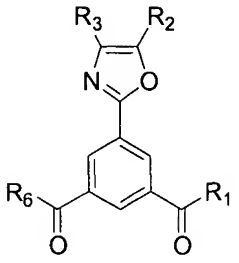
CLAIMS

What is claimed is:

1. A process for preparing a compound of the formula:



wherein:

R_1 is C_1-C_6 alkoxy or OH;

R_2 and R_3 are independently H, phenyl, or C_1-C_4 alkyl; or

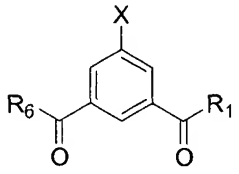
R_2 and R_3 and the carbons to which they are attached form a benzo ring, which is optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, or dialkylamino; and

R_6 is C_1-C_6 alkoxy or NR_4R_5; wherein

R_4 and R_5 are independently C_1-C_6 alkyl;

comprising:

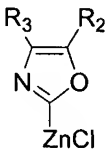
forming a reaction mixture comprising a compound of formula I:



I,

wherein X is Br, I, OTf, or OMs;

a compound of formula II:



II,

a catalyst and at least one solvent.

2. A process according to claim 1, wherein the catalyst is a transition metal catalyst.

3. A process according to claim 2 wherein the transition metal catalyst is $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $PdCl_2$, $PdCl_2$ and PPh_3, or $Pd(OCOCH_3)_2$.

4. A process according to claim 3, wherein the catalyst is $Pd(PPh_3)_4$.

5. A process according to claim 1 wherein the method is conducted in the presence of at one additional polar, aprotic solvent.

6. A process according to claim 5, wherein the polar, aprotic solvent is tetrahydrofuran, tetramethyltetrahydrofuran, glyme, methyl t-butyl ether, or a mixture thereof.

7. A process according to claim 6, wherein the polar, aprotic solvent is tetrahydrofuran.

8. A process according to claim 1, wherein the reaction is performed at a temperature of from about 25°C to about the refluxing temperature of the solvent used.

9. A process according to claim 8 wherein the temperature is about 30°C to about 75°C.

10. A process according to claim 9, wherein the temperature is about 40°C to about 60°C.

11. A process according to claim 10, wherein the reaction mixture is formed by combining I, II and the catalyst, and any additional optional additives, at once or within a short time of each other.

12. A process according to claim 10, wherein the reaction mixture is formed over a period of about 0.5 hours to about 4 hours.

13. A process according to claim 12, wherein the time is about 1 hour to about 3 hours.

14. A process according to claim 13, wherein the time is about 1.5 hours to about 2.5 hours.

15. A process according to claim 1 wherein the transition metal catalyst is present in 0.01 to 20 mole percent, based on the amount of the compound of formula I.

16. A process according to claim 15, wherein the transition metal catalyst is present in 0.1 to 10 mole percent, based on the amount of the compound of formula I.

17. A process according to claim 16, wherein the transition metal catalyst is present in 1 to 7 mole percent, based on the amount of the compound of formula I.

18. A process according to claim 17, wherein the reaction mixture is heated for about 24 hours.

19. A process according to claim 18, wherein the reaction mixture is heated for about 0.5 to about 8 hours.

20. A process according to claim 19, wherein the reaction mixture is heated for about 0.5 to about 4 hours.

21. A process according to claim 20, wherein the reaction mixture is heated for about 0.5 to about 2.25 hours.

22. A process according to claim 1, wherein the compound of formula II is used in an excess from 1.001 to 10 equivalents, based on the compound of formula I.

23. A process according to claim 22, wherein the compound of formula II is used in an excess from 1.01 to 5 equivalents, based on the compound of formula I.

24. A process according to claim 23, wherein the compound of formula II is used in an excess of 3 equivalents, based on the compound of formula I.

25. A process according to claim 1, wherein

X is Br;

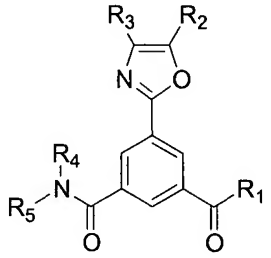
R_2 and R_3 are independently H, methyl or ethyl;

R_6 is NR_4R_5; wherein

R_4 and R_5 are both C_3 alkyl; and

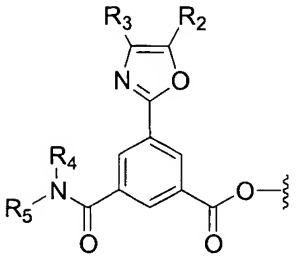
R_1 is C_1-C_4 alkyl.

26. A compound of the formula:



wherein:

R_1 is is OH, imidazolyl, halogen, $-OC(O)CH_3$, $-OC(O)CF_3$;



;

R_2 and R_3 are independently H or C_1-C_4 alkyl; and

R_4 and R_5 are independently C_1-C_6 alkyl.

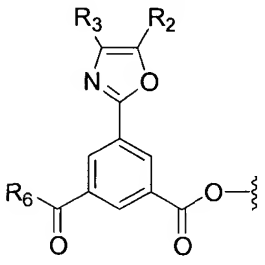
27. A compound according to claim 26, wherein R_2 and R_3 are independently H or methyl.

28. A compound according to claim 27, wherein R_4 and R_5 are both C_3 alkyl.

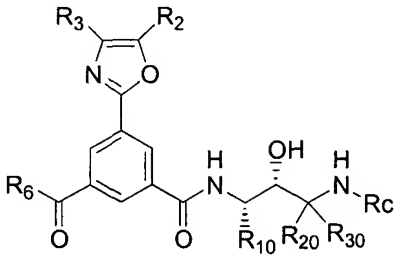
29. A compound according to claim 28, wherein R_1 is OH.

30. A compound according to claim 28, wherein R_1 is C_1-C_4 alkoxy.

31. A compound according to claim 28, wherein R_1 is chloro.

32. A compound according to claim 28, wherein R_1 is  .

33. A process for preparing compounds of the formula:



wherein

R_{10} is $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl), or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, -C≡N, $-CF_3$, $-C_1$-C_3 alkoxy, amino, mono- or

dialkylamino, -N(R)C(O)R'-, -OC(=O)-amino and -OC(=O)-mono- or dialkylamino, or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino, or

aryl, heteroaryl, heterocyclyl, $-C_1$-C_6 alkyl-aryl, $-C_1$-C_6 alkyl-heteroaryl, or $-C_1$-C_6 alkyl-heterocyclyl, where the ring portions of each are optionally substituted with 1, 2, 3, or 4 groups independently selected from halogen, -OH, -SH, -C≡N, $-NR_{105}R'_{105}$, $-CO_2R$, -N(R)COR', or $-N(R)SO_2R'$, $-C(=O)-(C_1-C_4)$ alkyl, $-SO_2$-amino, $-SO_2$-mono or dialkylamino, -C(=O)-amino, -C(=O)-mono or dialkylamino, $-SO_2-(C_1-C_4)$ alkyl, or

C_1-C_6 alkoxy optionally substituted with 1, 2, or 3 groups which are independently selected from halogen, or

C_3-C_7 cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, $-C_1$-C_6 alkyl and mono- or dialkylamino, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, $-C_1$-C_3 alkoxy, amino, mono- or dialkylamino and $-C_1$-C_3 alkyl, or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, C_1-C_6 alkyl and mono- or dialkylamino; and the heterocyclyl group is optionally further substituted with oxo;

R and R' independently are hydrogen, C_1-C_{10} alkyl, C_1-C_{10} alkylaryl or C_1-C_{10} alkylheteroaryl;

R_{20} is selected from the group consisting of H; C_1-C_6 alkyl, optionally substituted with 1, 2, or 3 substituents that are independently selected from the group consisting of C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$; $-(CH_2)_{0\text{-}4}$-aryl; $-(CH_2)_{0\text{-}4}$-heteroaryl; C_2-C_6 alkenyl; C_2-C_6 alkynyl; $-CONR_{N\text{-}2}R_{N\text{-}3}$; $-SO_2NR_{N\text{-}2}R_{N\text{-}3}$; $-CO_2H$; and $-CO_2-(C_1$-C_4 alkyl); wherein

$R_{1\text{-}a}$ and $R_{1\text{-}b}$ are independently -H or C_1-C_6 alkyl;

R_{30} is selected from the group consisting of H; C_1-C_6 alkyl, optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$; $-(CH_2)_{0\text{-}4}$-aryl; $-(CH_2)_{0\text{-}4}$-heteroaryl; C_2-C_6 alkenyl; C_2-C_6 alkynyl; $-CO-NR_{N\text{-}2}R_{N\text{-}3}$; $-SO_2-NR_{N\text{-}2}R_{N\text{-}3}$; $-CO_2H$; and $-CO-O-(C_1$-C_4 alkyl);

or

R_{20}, R_{30} and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from-O-, -S-, $-SO_2-$, or $-NR_{N\text{-}2}-$;

$R_{N\text{-}2}$ and $R_{N\text{-}3}$ at each occurrence are independently selected from the group consisting of $-C_1$-C_8 alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -OH, $-NH_2$, phenyl and halogen; $-C_3$-C_8 cycloalkyl; $-(C_1$-C_2 alkyl)-(C_3-C_8 cycloalkyl); $-(C_1$-C_6 alkyl)-O-(C_1-C_3 alkyl); -C_2-C_6 alkenyl; $-C_2$-C_6 alkynyl; $-C_1$-C_6 alkyl chain with one double bond and one triple bond; aryl; heteroaryl; heterocycloalkyl;

or

$R_{N\text{-}2}$, $R_{N\text{-}3}$ and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or heteroaryl group, wherein said heterocycloalkyl or heteroaryl group is optionally fused to a benzene, pyridine, or pyrimidine ring, and said groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that at

each occurrence are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -CN, $-NO_2$, $-NH_2$, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), -OH, $-C(O)NH_2$, $-C(O)NH(C_1$-C_6 alkyl), $-C(O)N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 thioalkoxy, and C_1-C_6 thioalkoxy C_1-C_6 alkyl;

R_C is hydrogen, $-(CR_{245}R_{250})_{0-4}$-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-aryl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-aryl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-aryl-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-aryl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-heteroaryl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-heteroaryl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-heterocyclyl, $-(CR_{245}R_{250})_{0-4}$-heterocyclyl-aryl, $-[C(R_{255})(R_{260})]_{1-3}$-CO-N-$(R_{255})_2$, $-CH(aryl)_2$, $-CH(heteroaryl)_2$, $-CH(heterocyclyl)_2$, -CH(aryl)(heteroaryl), $-(CH_2)_{0-1}$-CH($(CH_2)_{0-6}$-OH)-$(CH_2)_{0-1}$-aryl, $-(CH_2)_{0-1}$-CH($(CH_2)_{0-6}$-OH-$(CH_2)_{0-1}$-heteroaryl, -CH(-aryl or -heteroaryl)-CO-O(C_1-C_4 alkyl), -CH(-CH_2-OH)-CH(OH)-phenyl-NO_2, (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-OH; $-CH_2$-NH-CH_2-CH(-O-CH_2-CH_3)$_2$, $-(CH_2)_{0-6}$-C(=NR_{235})($NR_{235}R_{240}$), or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of R_{205}, $-OC{=}ONR_{235}R_{240}$, $-S(=O)_{0-2}(C_1$-C_6 alkyl), -SH, $-NR_{235}C{=}ONR_{235}R_{240}$, $-C{=}ONR_{235}R_{240}$, and $-S(=O)_2NR_{235}R_{240}$, or

$-(CH_2)_{0-3}$-(C_3-C_8) cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of R_{205}, $-CO_2H$, and $-CO_2$-(C_1-C_4 alkyl), or

cyclopentyl, cyclohexyl, or cycloheptyl ring fused to aryl, heteroaryl, or heterocyclyl wherein one, two or three carbons of the cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with a heteroatom independently selected from NH, NR_{215}, O, or $S(=O)_{0-2}$, and wherein the cyclopentyl, cyclohexyl, or cycloheptyl group can be optionally substituted with

one or two groups that are independently R_{205}, =O, $-CO-NR_{235}R_{240}$, or $-SO_2-(C_1-C_4$ alkyl), or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups, wherein

each aryl and heteroaryl is optionally substituted with 1, 2, or 3 R_{200}, and wherein each heterocyclyl is optionally substituted with 1, 2, 3, or 4 R_{210};

R_{200} at each occurrence is independently selected from -OH, $-NO_2$, halogen, $-CO_2H$, C≡N, $-(CH_2)_{0-4}-CO-NR_{220}R_{225}$, $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl), $-(CH_2)_{0-4}-CO-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-CO-$aryl, $-(CH_2)_{0-4}-CO-$heteroaryl, $-(CH_2)_{0-4}-CO-$heterocyclyl, $-(CH_2)_{0-4}-CO-O-R_{215}$, $-(CH_2)_{0-4}-SO_2-NR_{220}R_{225}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-O-R_{215}$, $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-N-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-N(-H$ or $R_{215})-CO-R_{220}$, $-(CH_2)_{0-4}-NR_{220}R_{225}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(OR_{240})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-O-(R_{215})$, $-(CH_2)_{0-4}-O-(R_{215})-COOH$, $-(CH_2)_{0-4}-S-(R_{215})$, $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with 1, 2, 3, or 5 -F), C_3-C_7 cycloalkyl, $-(CH_2)_{0-4}-N(H$ or $R_{215})-SO_2-R_{220}$, $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 R_{205} groups, or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl, each of which is optionally substituted with 1 or 2 R_{205} groups, wherein

the aryl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 groups that are independently R_{205}, R_{210}, or

C_1-C_6 alkyl substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

the heterocyclyl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently R_{210};

R_{205} at each occurrence is independently selected from C_1-C_6 alkyl, halogen, -OH, -O-phenyl, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, NH_2, NH(C_1-C_6 alkyl) or N-(C_1-C_6 alkyl)(C_1-C_6 alkyl);

R_{210} at each occurrence is independently selected from halogen, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $-NR_{220}R_{225}$, OH, C≡N, -CO-(C_1-C_4 alkyl), $-SO_2-NR_{235}R_{240}$, $-CO-NR_{235}R_{240}$, $-SO_2-(C_1-C_4$ alkyl), =O, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_7 cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups;

R_{215} at each occurrence is independently selected from C_1-C_6 alkyl, $-(CH_2)_{0-2}$-(aryl), C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and $-(CH_2)_{0-2}$-(heteroaryl), $-(CH_2)_{0-2}$-(heterocyclyl), wherein

the aryl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

the heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 R_{210};

R_{220} and R_{225} at each occurrence are independently selected from -H, $-C_3$-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), $-C_2$-C_6 alkenyl, $-C_2$-C_6 alkynyl, -C_1-C_6 alkyl chain with one double bond and one triple bond, -aryl, -heteroaryl, and -heterocyclyl, or

-C_1-C_{10} alkyl optionally substituted with -OH, $-NH_2$ or halogen, wherein

the aryl, heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 R_{270} groups

R_{235} and R_{240} at each occurrence are independently H, or C_1-C_6 alkyl;

R_{245} and R_{250} at each occurrence are independently selected from -H, C_1-C_4 alkyl, C_1-C_4 alkylaryl, C_1-C_4 alkylheteroaryl, C_1-C_4 hydroxyalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, -$(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and phenyl; or

R_{245} and R_{250} are taken together with the carbon to which they are attached to form a carbocycle of 3, 4, 5, 6, or 7 carbon atoms, where one carbon atom is optionally replaced by a heteroatom selected from -O-, -S-, -SO_2-, and -NR_{220}-;

R_{255} and R_{260} at each occurrence are independently selected from -H, -$(CH_2)_{1-2}$-S(O)$_{0-2}$-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-aryl, -(C_1-C_4 alkyl)-heteroaryl, -(C_1-C_4 alkyl)-heterocyclyl, -aryl, -heteroaryl, -heterocyclyl, -$(CH_2)_{1-4}$-R_{265}-$(CH_2)_{0-4}$-aryl, -$(CH_2)_{1-4}$-R_{265}-$(CH_2)_{0-4}$-heteroaryl, -$(CH_2)_{1-4}$-R_{265}-$(CH_2)_{0-4}$-heterocyclyl, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or -$(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups, wherein

each aryl or phenyl is optionally substituted with 1, 2, or 3 groups that are independently R_{205}, R_{210}, or

C_1-C_6 alkyl substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

each heterocyclyl is optionally substituted with 1, 2, 3, or 4 R_{210};

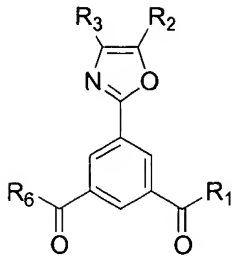
R_{265} at each occurrence is independently -O-, -S- or -N(C_1-C_6 alkyl)-;

R_{270} at each occurrence is independently R_{205}, halogen C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $NR_{235}R_{240}$, -OH, -C≡N, -CO-(C_1-C_4 alkyl), -SO_2-$NR_{235}R_{240}$, -CO-$NR_{235}R_{240}$, -SO_2-(C_1-C_4 alkyl), =O, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or -$(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups;

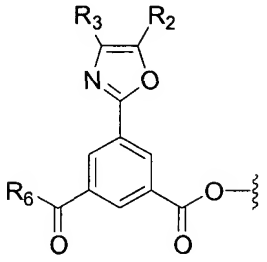
comprising

forming a reaction mixture comprising a compound of formula III



III

wherein

R_1 is OH, imidazolyl, halogen or  ;

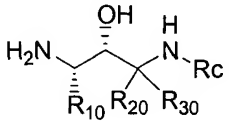
R_2 and R_3 are independently H, phenyl, or C_1-C_4 alkyl; or

R_2 and R_3 and the carbons to which they are attached form a benzene ring; and

R_6 is C_1-C_6 alkoxy or NR_4R_5; wherein

R_4 and R_5 are independently C_1-C_6 alkyl;

and a compound of formula VIII



VIII

in a solvent.

34. A process according to claim 33, wherein the solvent is selected from THF, DMF, CH_2Cl_2, and $CHCl_3$.

35. A process according to claim 35 wherein the reaction mixture comprises a base which is pyridine, collidine, di-tertiarybutyl pyridine, triethylamine, diisopropylethylamine, dimethylamino pyridine, or lutidine.

36. A process according to claim 35, wherein the reaction mixture further comprises an additive which is 1, 2, or 3 of the following:
EDCI, HOBT, benzotriazole, HOAT, HATU, or DCC.